REMARKS

Claim 1 has been amended to state that the limitation of "detecting an effect of [a] candidate drug compound on said target ion channel" is performed "while [the] target ion channel is subject to [a] set transmembrane potential level." Support for this amendment can be found, for example, in original Claim 1, ¶¶ [0206], [0207], [0375]-[0381], and [0494] of U.S. Pub. No. 2004/0191757. This amendment does not constitute new matter.

Applicants respectfully submit that the detection claimed above has not been produced or observed with the recited method prior to the present invention, and that the pending claims are in condition for allowance.

Claims 1, 2 and 4-6 are rejected under 35 U.S.C. §103(a) in light of Connolly et al. ("Connolly") and Catteral et al. ("Catterall"). Claims 1-6 are rejected under 35 U.S.C. §103(a) as unpatenable over Catterall and Connolly in view of Tung et al. ("Tung").

Amended Claim 1 is not obvious. Amended Claim 1 recites a "method of screening a plurality of drug candidate compounds against a target ion channel comprising ... modulating a transmembrane potential of host cells in said plurality of sample wells with a repetitive application of electric fields applied with extracellular electrodes so as to set said transmembrane potential to a level corresponding to a pre-selected voltage dependent state of said target ion channel; and detecting an effect of said candidate drug compound on said target ion channel while said target ion channel is subject to said set transmembrane potential level."

Independent Claim 1 is not obvious in view of Catterall and Connolly. As illustrated in Figures 10-13 of the instant application, transmembrane potentials are set to a level depending on applied voltage parameters. This setting of a transmembrane potential to a particular level is accomplished for a period of time long enough to detect an effect of a candidate compound on a target ion channel.

The Examiner cites Catterall as teaching the "modulation of a transmembrane potential of cells." Office Action of November 16, 2006 at 2. However, Catterall does not disclose or suggest the use of extracellular electrodes.

The Examiner cites Connolly as providing motivation for using extracellular electrodes to perform the methods described in Catterall. Connolly, however, does not provide such

motivation. At the time of Applicants' invention, patch clamping methods were used for manipulation of transmembrane potentials. Connolly does not suggest differently. The presence of extracellular electrodes in Connolly were merely used to initiate beating of cardiac cells (Connolly at page 232), and there is no suggestion that the extracellular electrodes could have been used to produce the claimed effect. At the time of Applicants' invention one of ordinary skill in the art relied on patch clamping techniques and would not have considered the techniques of extracellular electrodes in Connolly. Thus, Connolly does not provide the motivation the Examiner asserts. A technique that used extracellular electrodes to set a transmembrane potential to a certain level was unknown at the time of Applicants' invention and Connolly does not provide a motivation for one of ordinary skill in the art to combine extracellular electrodes with the method of Caterall.

The Examiner notes that Tung states that "electrical stimulation of cardiac cells by imposed exracellular electric fields results in a transmembrane potential which is highly non-uniform." By stating that extracellular electrodes produced highly non-uniform transmembrane potential levels Tung teaches away from the use of extracellular electrodes to successfully and consistently manipulate transmembrane potential levels. The Examiner notes that despite the teaching of Tung, "this does not mean that any of the transmembrane potentials being imposed do not correspond to a pre-selected voltage dependent state." Office Action of November 16, 2006 at 2. However, Tung, does not suggest any ability to test compound effect while the target ion channel is subject to the set potential. The Examiner also argues that although Catterall and Connolly do not disclose repetitive application of biphasic electric fields, but that Tung remedies this deficiency. However, because Tung teaches away from using extracellular electrodes to perform cell stimulation, there is no motivation to combine Catterall, Connolly and Tung. Thus, Catterall, Connolly and Tung do not render Claim 1 (or the claims dependent therefrom) obvious.

Claims 1, 2, and 4-7 are also rejected under 35 U.S.C. § 103(a) as unpatentable over *Catterall* and *Connolly* in view of *Tsien et al.* or *Denyer et al.* The Examiner states that "*Tsien et al.* and *Denyer et al.* are combined with *Catterall et al.* and *Connolly et al.* only to teach the use of voltage sensors."

As noted above, amended Claim 1 is not obvious in light of *Catterall* and *Connolly*. Neither *Tsien* nor *Denyer* remedies that deficiency. Indeed, the Examiner cites *Tsien* and *Denyer* "only to teach the use of voltage sensors." While *Tsien* stimulates a transmembrane electrical potential with chemical stimulation and *Denyer* discloses ion channel assays with radio tracers, neither *Tsien* nor *Denyer* renders obvious a combination of *Catterall* and the extracellular stimulation of *Connolly*. Thus, Applicants respectfully request that the Examiner's rejection of Claim 1 on this basis be withdrawn.

Claims 2-7 are dependent on Claim 1, and it is respectfully submitted that these claims are also patentable for at least the same reasons as set forth above with regard to Claim 1.

CONCLUSION

The Applicants have endeavored to address all of the Examiner's concerns as expressed in the previous Office Action. Accordingly, arguments in support of the patentability of the pending claim set are presented above. In light of these amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested.

If any issues remain that could be resolved by telephone, the Examiner is invited to call the undersigned directly. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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By: _____

Thomas R. Arno
Registration No. 40,490
Attorney of Record
Customer No. 20,995
(619) 235-8550

3055184
102606